## REMARKS

The rejection under 35 U.S.C. § 112, first paragraph

The examiner rejected claims 3 and 6-9 under 35 U.S.C. § 112, first paragraph, arguing that the specification does not enable a method for preventing death or degeneration of neural cells. The applicants have amended claim 3 such that it does not recite the limitation "prevent," and have canceled claims 6-9. The Applicants submit that the enablement rejection is not moot, and respectfully request that the examiner withdraw it.

The rejection of claim 10 under 35 U.S.C. § 103(a)

The Examiner rejected claim 10 under 35 U.S.C. § 103(a), arguing that the claim is obvious. The applicants have canceled claim 10. The applicants submit that the obviousness rejection is now moot, and respectfully request that the examiner withdraw it.

The provisional double patenting rejection

The examiner provisionally rejected claims 1-2, 4-5, and 11-13 under the doctrine of obvious-type double patenting, arguing that the claims are not patentably distinct from the claims 4-6 and 8-9 of copending application US 10/881,761. The applicants respectfully disagree that the rejection is proper.

Claims 4-6 and 8-9 of the co-pending application are directed to methods of treating a neurodegenerative condition in a mammal, comprising the coadministration of a first component comprising a compound whose activity results in a direct or indirect activation of the alpha-2 adrenergic receptor, and a second component comprising an alpha-1 adrenergic receptor antagonist. As the examiner states, brimonidine is an alpha-2 agonist. But in the case of the present application, brimonidine is administered alone.

The difference between the method of the present invention, and the method of the co-pending claims, is that coadministering an alpha-1 antagonist makes it possible to use higher doses of the alpha-2 agonist without sedation. As the co-pending application describes, this effect is dramatic:

> As shown in FIG. 1, in the sulprostone-induced mouse model intraperitoneal administration of the alpha 1 antagonist 5-methyl urapidil at a dose of 30 µg/kg 5 minutes before administration of the clonidine shifts the effective analgesic dose 10-fold lower than the dose response using clonidine alone (see FIG. 1), while leaving the sedating dose unchanged (See FIG. 2). Thus, co-administration of clonidine (an alpha 2 agonist) and an alpha 1 antagonist causes a "widening" of the therapeutic window between pain and sedation from 3-10 fold to approximately 30-100 fold in a model of chronic pain.

At ¶ 90. Co-administering an alpha-2 agonist and alpha-1 antagonist also increased the potency of the alpha-2 agonist in another experiment, causing the alpha-2 agonist to relieve pain at doses it was ineffective at relieving pain when administered alone. *Id.*, at 97 ("the administration of [clonidine] and alpha 1 antagonist again resulted in an increase in the potency . . . the 0.1 microgram dose of clonidine is not analgesic in the absence of prazosin.").

As the data indicate, administering brimonidine alone is vastly different from administering an alpha-2 agonist together with an alpha-1 antagonist. For this reason, the applicants submit that the methods of the present application and co-pending application are patentably distinct, and the respectfully request that the examiner withdraw the provisional double-patenting rejection.

The undersigned authorizes the Director to charge any fees required or necessary for the filing, processing or entering of this paper or any of the papers transmitted with it, and to refund any overpayment, to deposit account 01-0885.

Respectfully submitted,

March 25, 2009 /Joel B. German/

Joel B. German, Esq.
Attorney of Record
Registration No. 48,676

Please direct all correspondence and inquires to:

Joel B. German, Esq.
Allergan, Inc.
2525 Dupont Drive, T2-7H
Irvine, CA 92612
Tel: (714) 246- 4920
Fax: (714) 246-4249